

Symposium: Biophysics in Industry: Putting Evolution in Practice

2137-Symp

Transforming Yeast from Moonshiners into Oil Barons

Timothy Gardner.

Amyris, Inc., Emeryville, CA, USA.

Amyris has transformed ethanologenic baker's yeast into farnesene oil producers. Farnesene is a 15-carbon hydrocarbon derived from the sterol synthesis pathway (the same root pathway that make cholesterol). Its branched structure makes it ideal for processing into base-oils for cosmetics (replacing shark liver oil), synthetic engine lubricants, diesel fuel, and high-performing polymers for tires. In four years, Amyris has improved its yeast from producing only a single microliter in a test tube, to making thousands of liters in a full-scale fermentations at unprecedented yields and productivities. I will share lessons learned from the challenges of strain development and scale-up at Amyris, and how those lessons might be applied to accelerate and empower research in Industrial Biotechnology.

2138-Symp

Harnessing Nature's Diversity for Production of Unique Triglyceride Oils

Peter Licari.

Solazyme, Inc., South San Francisco, CA, USA.

Solazyme, Inc. is a renewable oil and bioproducts company that transforms a range of low-cost sugars into high-value tailored triglyceride oils. Solazyme's renewable products can replace or enhance the properties of oils derived from the world's dominant sources: petroleum, plants, and animals.

Our technology is comprised of a robust biotechnology platform employing homologous recombination in microalgae. Precise gene insertion results in both temporal and spatial regulation of gene expression in this system. By feeding sugars to these optimized strains of microalgae in a heterotrophic fermentation process, we are able to produce tailored oils with high yields and productivities. We utilize standard industrial fermentation and vegetable oil processing equipment to efficiently scale, recover, and purify valuable oils.

Solazyme is able to generate oil compositions that the world has never seen before by taking advantage of nature's diversity and mining specific oil biosynthetic enzymes. We have produced tailored oils with dramatically altered chain length, saturation levels, and precise control of the regio-specificity of fatty acids on the glycerol backbone. The biology of our oil production process separates oil production from cell growth, allowing for the production of high concentrations of very unique oils that are not feasible in traditional oilseed crops. Solazyme's platform is directed at producing oils that are designed to meet specific industry needs, impacting many food and industrial applications because they have performance and functionality benefits that far surpasses what is commercially available today.

2139-Symp

Physical Constraints on Proteomes Impose Limits to Biological Evolution

Kenneth Dill.

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The main biomass in a cell is its proteome, its complement of all its proteins. So, it follows that many physical properties of the cell derive from the physical properties of the cell's proteins. Many physical properties of proteins in vitro and captured in databases. We combine that data with simple models of protein physics to draw inferences about the limits to the behaviors and evolution of cells. For example, the thermal properties of cells appear to depend on protein stabilities; cell growth rates depend on the speed of protein diffusion; and protein oxidation, which is associated with diseases and aging, can affect protein charge distributions.

Symposium: Mechanosensing in Eukaryotes

2140-Symp

Zen and the Art of Mechanosensation: How MscS-Like Mechanosensitive Channels Help Eukaryotic Cells and Organelles Reduce Stress

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A long-standing problem is how biological systems sense and perceive mechanical signals such as osmotic pressure, gravity, and touch. One well-established molecular mechanism for force sensing is the activation of mechanosensitive (MS) ion channels. The Mechanosensitive channel of Small

conductance (MscS) from *E. coli* functions as a hypo-osmotic safety valve, opening in response to increased membrane tension and preventing cellular rupture. Genes predicted to encode MscS homologs are found in genomes from all three kingdoms of life. We have been characterizing the structure, function, and regulation of ten MscS-Like (MSL) proteins in the model plant *Arabidopsis thaliana*. Based on their modest homology to MscS and high topological diversity, we have proposed that MSLs might (1) sense and respond to sources of membrane tension other than environmental hypo-osmotic stress; (2) be regulated by mechanisms in addition to membrane tension; and (3) signal in ways that are separable from ion flux. Evidence in support of all three of these hypotheses will be presented.

2141-Symp

May the Force Be with You: Search for Ion Channels that Respond to Pressure

Ardem Patapoutian.

TSRI/HHMI, La Jolla, CA, USA.

Mechanotransduction is perhaps the last sensory modality not understood at the molecular level. Proteins/ion channels that sense mechanical force are postulated to play critical roles in sensing touch/pain (somatosensation), sound (hearing), sheer stress (cardiovascular tone), etc.; however, the identity of ion channels involved in sensing mechanical force has remained elusive. We have recently identified Piezo1 and Piezo2, mechanically-activated cation channels that are expressed in many mechanosensitive cell types. Current efforts focus on understanding structure-function relationship of Piezo proteins, elucidating their physiological roles in various biological processes and diseases that depend on mechanotransduction, and identifying novel mechanical sensors.

2142-Symp

Touch as a Matter of Fat: The Phospholipids and DEG/ENaC Channels Needed for Metazoan Touch Sensation

Miriam B. Goodman.

Molecular and Cellular Physiology, Stanford University, Stanford, CA, USA.

Mechano-electrical transduction (MeT) channels are activated by mechanical energy and conduct ions across cell membranes. Such channels enable somatosensory neurons in our skin, joints, and muscles to monitor external touch and self-movement and to detect noxious inputs that initiate pain sensation. They also enable visceral sensory neurons such as baroreceptors to regulate heart function on a beat-by-beat basis. Genetic dissection in roundworms, fruitflies, and mice has led to the identification of many of the proteins that form MeT channels, including members of the TRP family of cation channels, DEG/ENaC sodium channels, and Piezo cation channels. This talk will present evidence establishing that DEG/ENaC sodium channels play crucial roles in both touch and nociception (O'Hagan et al, Nat Neurosci, 11:543, 2005; Geffeney et al, Neuron 71:845, 2011), highlighting aspects of the biophysics of MeT channel activation shared across neurons, species, and protein partners. To learn more about the physical basis of MeT channel activation in living sensory neurons, we are investigating the role of fatty acids and lipids in this process. Through a combination of genetic dissection and chemical complementation, we have identified specific poly-unsaturated phospholipids essential for normal touch sensation. We have also investigated how such lipids contribute to membrane mechanics. Collectively, our results support a model in which mechanosensitivity is a function not only of the proteins that form eukaryotic MeT channels, but also of the surrounding plasma membrane. Support: NIH NS047715; EB006745; AHA and HFSP Postdoctoral Fellowships.

2143-Symp

TMC Function in Hair Cell Mechanotransduction

Jeffrey R. Holt.

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Sensory hair cells of the mammalian inner ear convert sound stimuli and head movements into electrical signals that are transmitted to the brain. The molecules and mechanisms of sensory transduction in inner ear hair cells have been the focus of considerable interest and investigation. Recently, we identified Transmembrane channel-like proteins 1 and 2 (TMC1 and TMC2) as components of the mechanosensitive ion channels in hair cells. The data suggest that TMC1 or TMC2 are required for hair cell transduction and that expression of either one is sufficient to retain mechanosensitivity. Although these molecules are somewhat redundant in their function, there are clear differences in the biophysical properties of mechanotransduction in hair cells that express only TMC1 or only TMC2. The biophysical differences include differences in the rate and extent of adaptation, differences in calcium permeability and differences in single-channel conductance. Wild-type hair cells that express both TMC1 and TMC2 have a broad range of single-channel